American Journal of Hematology 58:239–240 (1998)

Chronic Lymphocytic Leukemia Remission Following Extra Corporeal Shock Wave Lithotripsy for Urinary Calculi

Alex E. Denes,[1] Arieh L. Shalhav,[2]* Gabor Kovacs,[2] and Ralph V. Clayman[2]

[1]Division of Hematology and Oncology, St. John's Mercy Medical Center, and Division of Medicine, Washington University School of Medicine, St. Louis, Missouri

[2]Division of Urology, Washington University School of Medicine, St. Louis, Missouri

Herein we report on a patient with chronic lymphocytic leukemia (CLL) who entered a long-term remission following shock wave lithotripsy (SWL) for a left proximal ureteral stone. In addition, we include data on the effect of SWL on in vitro and in vivo human lymphocyte subpopulations, and discuss the possible mechanisms of this observation. Am. J. Hematol. 58:239–240, 1998. © 1998 Wiley-Liss, Inc.

Key words: chronic lymphocytic leukemia; renal lithiasis; extra corporeal shock wave therapy

INTRODUCTION

Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in Europe and the United States. Although chemotherapy with alkylating agents, purine analogs, and corticosteroids often induces temporary remissions, the disease remains incurable with current treatment approaches and spontaneous remission is extremely rare [1].

Extracorporeal shock wave lithotripsy (SWL) has become the principle treatment modality for renal calculi. In vitro effects of SWL on blood cells include a dose-dependent mild red cell hemolysis but demonstrate no known effect on lymphocytes as determined by mixed lymphocyte culture and the lymphocyte proliferation index [2]. Clinically, SWL is known to cause renal tubular cell injury (as evidence by a rise in serum intracellular enzymes) and a transient leukocytosis [3]. Of interest, SWL has been reported to impair the viability of cancer cells in suspension [4].

Herein we report on a patient with CLL who entered a long-term remission following SWL for a left proximal ureteral stone. In addition, we include data on the effect of SWL on in vitro and in vivo human lymphocyte subpopulations, studies that were stimulated by this original observation.

CASE REPORT

A 52-year-old white male with Rai stage 1, B cell CLL diagnosed in May 1994, presented in August 1995 with renal colic caused by a 10 × 4 mm left proximal ureteral stone. On August 3, 1995, he underwent SWL using the Lithostar Plus lithotripter; he received 8,500 shocks at an average kV of 18.1. Follow-up showed resolution of the stone.

Bone marrow biopsy at diagnosis of CLL showed 85% involvement and his WBC was consistently in the range of 54,000/μL to 71,000/μL. The patient never received any treatment for CLL, as dictated by his disease stage. Immediately prior to SWL, his WBC was 69,200/μL with 91% lymphocytes. Three months following SWL, his WBC decreased to 18,230/μL. This was associated with a resolution of palpable cervical adenopathy. A bone marrow biopsy performed 10 months after SWL showed 20–25% residual involvement by CLL. At 1.5 years after SWL, his WBC was 3,600/μL with 36% lymphocytes and flow-cytometry for circulating CD5 positive B cells was within normal limits. He is

*Correspondence to: A.L. Shalhav, M.D., Box 8242, Washington University School of Medicine, Division of Urology, 4960 Children's Place, St. Louis, MO 63110. E-mail: shalhava@msnotes.wustl.edu

Received for publication 2 March 1998; Accepted 18 March 1998

now 2.3 years after SWL; his WBC is 4,700/μL with 24% lymphocytes. There is no palpable lymphadenopathy and he remains asymptomatic.

DISCUSSION

In order to investigate the potential role of SWL in inducing remission in this patient, we evaluated the in vitro effect of SWL on peripheral blood from CLL patients; 10 cc peripheral blood from 9 CLL patient were treated with SWL in vitro. Using an HM-3 Lithotripter, a total of 30 shocks was given at 18 KV, as we calculated this would be the amount of energy incident on 10 cc circulating blood during an average SWL. The control was 10 cc of peripheral blood from the same patient, that underwent the same radiation exposure for localization and the same immersion time in 37°C water, but no shock waves were delivered. No differences between the study and control group were observed in the CBC, differential, or flow-cytometry determined lymphocyte immunophenotype with or without SWL. This demonstrates that significant mechanical destruction of circulating lymphocytes or leukemia cells during SWL likely does not occur.

In the second phase, we studied the in vivo effects of SWL on the normal lymphocyte population. Peripheral blood from 10 patients with urinary stones was obtained before, 2 hr after, and 2 weeks after SWL. These patients had no history of hematologic malignancy. CBC, differential, and flow cytometry studies before and after SWL showed no differences in 9 patients. This suggests that SWL has no effect on normal lymphocyte populations. One patient, with a normal preoperative CBC, had baseline elevation of CD19+CD5+lymphocytes (33%), which normalized 2 weeks after treatment. The observation in this patient is intriguing since this is the same phenotype that accumulates in CLL.

Spontaneous remission of CLL is an extremely rare event with only 39 reported cases [1,5,6]. The mechanism for this remission is unknown. However, upper respiratory infection, viral infection, small pox vaccination, and bilateral orchitis preceded spontaneous remission in 8 of the 39 patients (21%). Of interest, in 6 patients a second epithelial neoplasm developed before or during documented spontaneous remission [1,5]. According to these observations, it is hypothesized that spontaneous remission in CLL is the result of an altered host-tumor relationship [5]. The delay observed between clinical and ''clonal'' remissions as observed by Ribera et al. (0.9–1.8 years) [1] and in our patient (1.5 years) suggests an immunomodulatory rather than a cytotoxic effect.

Possible mechanisms by which SWL may have affected the CLL in our patient include mechanical damage to a susceptible cell line with removal of injured cells from the circulation and/or immunogenic response to intracellular humoral factors released from injured circulating or splenic CLL cells, which in turn, induce a host immune defense mechanism towards the CLL cells. However, the fact that the response was durable for >2 years most strongly supports the last option.

We are now about to initiate clinical studies to determine whether SWL can induce remission in patients with CLL.

REFERENCES

1. Ribera J, Vinolas N, Urbano-Ipizua A, Montserrat E, Rozman C: Spontaneous complete remission in chronic lymphocytic leukemia: report of three cases and review of the literature. Blood Cells 12:471–480, 1987.
2. Chaussy C, Brendel W, Schmiedt E: Extracorporeally induced destruction of kidney stones by shock waves. Lancet 1:1265–1268, 1980.
3. Haupt G, Haupt A, Donovan JM, Drach GW, Chaussy C: Short term changes after ESWL: A comparative study. J Urol 142:259–262, 1989.
4. Marcus M, Long S, Denstedt J, Clayman RV: Biomechanical effects of ESWL: Relation of applied voltage and shockwave number to cell viability and stone fragmentation. J Endourol 4:301–302, 1990.
5. Tin Han: Spontaneous remission in chronic lymphocytic leukemia: An update. Blood Cells 12:481–483, 1987.
6. Holmes JA, Whitaker JA: Spontaneous remission in chronic lymphocytic leukemia. Br J Haematol 69:97–99, 1988.